REMARKS

Rejection of Claims 45-48, 50-51 and 53-54 Under 35 U.S.C. §103(a)

Claims 45-48, 50-51 and 53-54 are rejected under 35 U.S.C. §103(a) as being unpatentable over Kwon et al., in view of Taunton et al., Baracchini et al., and Bennett et al.

Applicants again would like to point out that the instant claims **are not** directed to antisense oligonucleotides. Rather Claims 45-48, 50-51 and 53-54 are directed to an agent that inhibits one or more specific histone deacetylase isoforms, but less than all histone deacetylase isoforms, wherein the agent is a histone deacetylase **small molecule inhibitor**.

As such, one skilled in the art of small molecule chemistry would not have been motivated by the teachings of Taunton et al., Baracchini et al., and Bennett et al., alone or in combination, to do anything, much less to obtain the instantly claimed invention. Therefore, Taunton et al., Baracchini et al., and Bennett et al. are irrelevant to the instantly claimed invention. Accordingly, the question remains whether Claims 45-48, 50-51 and 53-54 are patentable over Kwon et al.

As argued in response to the previous Office Action, Kwon does not teach or suggest that depudecin inhibits "one or more specific histone deacetylase isoforms, but less than all histone deacetylase isoforms". The Office Action continues to assert that HDAC-1 is the only isoform used in the reference; however, this is simply in error. While it is true that some of the assays use recombinant FLAG epitope tagged HDAC1 there is nothing which teaches that depudecin inhibits only HDAC1. The PTO cannot ignore the full teachings of the Kwon reference especially that several assays use crude cell extracts which measures total HDAC activity and not just HDAC1.

Thus, Kwon compares depudecin activity to trichostatin A and trapoxin activity, two pan-inhibitors of HDAC (i.e., inhibit all isoforms). As taught by Kwon, depudecin shares common target proteins with trapoxin (see Kwon, "[^{3}H] Trapoxin Binding Assays" using extracts, pg 3358). Moreover, Kwon teaches that "it is known that inhibition of this activity by trichostatin A, trapoxin, and sodium butyrate results in the accumulation of hyperacetylated histone species." Kwon goes on to state that, as shown in Fig. 5, depudecin induces hyperacetylation of histones in a dose-dependent manner and that trichostatin A also strongly induces hyperacetylation of histones (see Kwon, "Depudecin induces Histone Hyperacetylation *in vivo*" using extracts, pgs 3358-3359. Finally, Figure 6A shows that in an assay testing the inhibitory activity of a

compound against a total cellular extract of cellular HDACs, depudecin inhibited the total cellular HDAC activity in a dose-dependent manner and that trichostatin A also showed strong inhibition (page 3359, left column, last paragraph; Figure 6A). No plateau for total cellular HDAC inhibition is demonstrated, taught or suggested in the Figure 6A or anywhere in the reference (i.e., if depudecin was inhibiting only HDAC1, one skilled in the art would expect a leveling off of inhibition demonstrated by activity of non-inhibited HDACs). Therefore, one of skill in the art would expect that increasing the dose of depudecin would result in increasing in the inhibition of HDAC activity in the cell extract. In other words, from the teachings of Kwon et al., one of skill in the art would come to the conclusion that depudecin is a pan-inhibitor of HDACs.

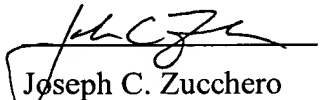
Thus, Claims 45-48, 50-51 and 53-54 are patentable over Kwon et al. Reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

Dated: December 16, 2008

By: 

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